REMARKS

Claims 1, 3-7, 11, 13, 17-19, 29, 37, 40-42, 46, 47, 56-58, 60-63, 67 and 68, as amended, and new claims 69-72, are pending in this application for the Examiner's review and consideration. Claims 1, 37 and 60 have been amended to recite preferred embodiments, i.e., the active agent is testosterone present in the amount of about 1% or less by weight of the formulation, support for which is found in the specification, e.g., paragraphs [0095], [0097], [0098], [0107]-[0111] and [0113]-[0124] of the published application, as well as claims 64 and 66, which have been cancelled. Claims 3, 17-20, 61, 67 and 68 were amended to be consistent with the pervious amendments. New claims 69-72 are directed to the most preferred embodiments, i.e., the delivery vehicle comprising ethanol, propylene glycol and monoethyl ether of diethylene glycol, support for which is found in the specification, e.g., paragraph [0107] and Table 5 of the published application. Claims 60 and 61 have been amended to avoid redundancy over other claims by removing the feature that the formulation is a gel. Claims 8-10, 15, 16, 20-26, 30, 31, 43-45, 59 and 65 have been cancelled without prejudice. Applicants reserve the right to present cancelled claims in a continuation or divisional application. As no new matter is introduced by these changes or additions, they should all be entered at this time.

Claims 1, 3-8, 10, 11, 13, 15, 20, 22, 37, 40-43, 45-47, 56, 57, 60-62 and 68 have been rejected under 35 U.S.C. 102(a) as allegedly being anticipated by International Patent Application Publication No. WO 02/22132 to Gray et al. (US Patent No. 7,030,104 is the English-language equivalent and relied upon by the Office Action, referred to hereinafter as "Gray"). Applicants respectfully disagree.

Gray relates to a topical hormonal composition comprising as active ingredients, a progestogen derived from 19-nor progesterone and estradiol or one of its derivatives, a vehicle which allows the systemic passage of said active ingredients, chosen from the group constituted by a solubilizing agent, an absorption promoting agent, a film-forming agent, a gelling agent and their mixtures, in combination or in a mixture with suitable excipients for the realization of a gelled and/or film-forming pharmaceutical form.

In contrast, the present claims as amended are now specifically directed to a formulation containing testosterone as the active agent, or method of use thereof, or a kit containing such a formulation. Therefore, Gray does not teach each and every element of the present claims as amended. Thus, the anticipation rejection over Gray should be withdrawn.

Claims 1, 3-11, 13, 15-26, 29-31, 37, 40-43, 45-47,56, 57, 60-62 and 68 have been rejected under 35 U.S.C. 103(a) as unpatentable over Gray and further in view of US Patent No. 6,503,894 to Dudley et al. (referred to hereafter as "Dudley"), US Patent No. 5,955,455 to Labrie et al. (referred to hereafter as "Labrie"), an article by Catherino et al. (J. Steroid Biochem. Molec. Biol., 1995, referred to hereinafter as "Catherino") and an article by Wang et al. (the Journal of Clinical Endocrinology and Metabolism, 2000, referred to hereinafter as "Wang").

As explained above, Gray does not teach or suggest the present claims as amended. The newly cited secondary references, Dudley, Labrie, Catherino and Wang, do not remedy the deficiencies of Gray.

Dudley relates to a pharmaceutical composition useful for treating hypogonadism comprising an androgenic or anabolic steroid, a C1-C4 alcohol, a penetration enhancer such as isopropyl myristate, and water.

Labrie teaches the treatment of vaginal atrophy, hypogonadism, diminished libido, loss of collagen or connective tissues in the skin using sex steroid precursors such as dehydroepiandrosterone and dehydroepiandrosterone sulphate.

Catherino discloses that megestrol acetate and nomegestrol acetate differ only at the 19 position, and that nomegestrol is a clinically useful progestin and an effective contraceptive agent when used as an implant.

Wang discloses packaging hydroalcoholic gels containing 1 wt.% testosterone in a multidose bottle with an actuator pump for treatment of hypogonadal males.

First of all, there is no teaching or suggestion in either reference to motivate a person of ordinary skill in the art to replace the active agents in the composition of Gray, i.e., progestogen derived from 19-nor progesterone and estradiol or one of its derivatives, with an androgenic or anabolic steroid disclosed in Dudley, as suggested by the Examiner. Importantly, Gray is specific for cutaneous topical preparations containing a synthetic progestogen and a natural or synthetic estrogen. Therefore, a person of ordinary skill in the art, following the teachings of Gray, will not choose to replace its active agents with testosterone mentioned by Dudley.

Moreover, there is no expectation of success to replace progestogen and estradiol taught in Gray with testosterone disclosed in Dudley. As supported by a previously submitted research paper (P. Karande et al., *High Throughput Screening of Transdermal Formulations*, Pharmaceutical Research, vol. 19, no. 5, May 2002, pp. 655-660), more than 200 chemical

enhancers including surfactants, fatty acids, fatty alcohols, and organic solvents have been used in attempts to increase transdermal drug transport. Dudley discloses that fatty acid derivatives, in particular, isopropyl myristate, are preferred penetration enhancers for the testosterone formulation (see the AndroGel® formulation in Table 5 of Dudley). Even though Dudley does mention other compounds such as diethylene glycol monomethyl ether in his listing of permeation enhancers, he attributes no preference to that compound. Thus, one of ordinary skill in the art, reading Dudley, will not be taught or motivated to select diethylene glycol monomethyl ether as taught in Gray in place of isopropyl myristate as the transdermal enhancer for the active agent testosterone as presently claimed. Furthermore, Dudley does not even mention diethylene glycol monoethyl ether as recited in claims 69-72.

Therefore, there is no motivation for one of ordinary skill in the art to combine the compositions of Gray and Dudley as suggested by the Examiner. Such a combination is only made possible by relying on the disclosure of the present application. The determination of obviousness is not whether a person could, with full knowledge of the present invention, reproduce it from prior art. The question is whether it would have been obvious, without knowledge of the present disclosure, to produce the same formulations that are presently claimed. This judgment cannot be made with the benefit of hindsight and Applicants submit that it is improper to take isolated disclosures from other formulations and change them in light of the now-known template of the present application, unless there is some direction in the prior art that would suggest this or that would clearly motivate a skilled artisan to do so. As no such motivation, teaching or suggestion exists in the cited references, the presently claimed invention is not obvious in view of Gray and Dudley along with the other secondary references. As the cited references do not render the present claims obvious, the rejection should be withdrawn.

Accordingly, it is believed that the entire application is now in condition for allowance, early notice of which would be appreciated.

Respectfully submitted,

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